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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/563,498	06/07/2006	Siegfried Ansorge	013183.00055	1382

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EXAMINER	
HA, JULIE	

ART UNIT	PAPER NUMBER
1654	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/563,498	ANSORGE ET AL.	
	Examiner	Art Unit	
	JULIE HA	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13 and 15-24* is/are pending in the application.

4a) Of the above claim(s) *1-4,6-12,15-21 and 23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5,13,22,24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 26, 2009 has been entered. Claims 1-13 and 15-24 are pending in this application. Applicant elected Group II and species (Lys[ZNO_2]thiazolidide) as DP IV inhibitor, actinonin as the APN inhibitor, benign fibrotic and sclerotic diseases as the species of diseases, oral as the systemic application, and creams as the topical application in the reply filed on January 17, 2008. Applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election was treated as an election without traverse. The restriction requirement was deemed proper and made FINAL in the previous office action. Claims 1-4, 6-12, 15-21 and 23 remain withdrawn from further consideration, as being drawn to nonelected inventions and species. Claims 5, 13, 22 and 24 are examined on the merits in this office action.

Withdrawn Rejection

2. Claims 5 and 13 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description, is hereby withdrawn in view of Applicant's amendment to the claims.

Maintained and Revised Rejection

35 U.S.C. 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 5, 13, 22 and 24 remain rejected under 35 U.S.C. 102(b) as being anticipated by Ansorge (WO 02/053170 (published July 11, 2002), machine translation used) as evidenced by Andriessen et al (Journal of Pathology, 1998, 186: 192-200) or Machesney et al (American Journal of Pathology, 1998, 152(5): 1133-1141) or Castagnoli et al (Clin. Exp. Immunol., 1990, 82: 350-354).

The instant claim is drawn to a method utilizing the inhibitor combinations (DPIV inhibitor and APN inhibitor) for treatment of benign fibrotic and sclerotic diseases, wherein therapy comprises an inhibition of activation, DNA synthesis and proliferation of human fibroblasts.

Ansorge et al teach the combined used of DP IV inhibitor (Lys[Z(NO_2)]thiazolidide) and APN inhibitor (actinonin) for the treatment of atherosclerosis and dermatological diseases (see paragraph 5 of the translated document). Furthermore, the reference teaches simultaneous administration of inhibitors and the administration is as topical application in the fore of creams, ointments, pastes, gels, solutions, spray, liposomes and systemic application to the oral, transdermal, intravenous, subcutaneous, intracutaneous, intramuscular with

pharmaceutically acceptable carrier (see paragraphs 6 and 9 of the translated document). Since the elected compound is taught by the reference and is disclosed that the compound can be used to treat dermatological diseases. The reference teaches the treatment of atherosclerosis, which is a species of sclerosis. The reference teaches that the combination therapy utilizing dermatological illnesses by inhibition of DNA synthesis, meeting the limitation of claims 5, 13, 22 and 24. Therefore, since Ansorge reference teaches the use of DP IV inhibitor (Lys[Z(NO_2)]thiazolidide) and APN inhibitor (actinonin) to treat dermatological diseases (associated with hyperproliferation of keratinocytes), this administration would treat other benign fibrotic and sclerotic diseases. Andriessen et al teach that hypertrophic scarring revealed an increase in basal keratinoctye proliferation rate (se abstract and Discussion), indicating that keratinocytes are involved in hypertrophic scarring. Furthermore, Machesney et al teach that keratinocytes play roles in hypertrophic scar epidermis (see abstract and Discussion). Castagnoli et al further teaches that sections from all hypertrophic scars showed an anomalous expression of HLA-DR molecules on keratinocytes and fibroblasts, further showing evidence that both keratinoctyes and fibroblasts are involved in hypertrophic scars (benign fibrotic and sclerotic diseases). Therefore, the reference meets the limitations of claims 5, 13, 22 and 24.

Response to Applicant's Arguments

5. Applicant argues that "the present claims are distinct from the reference of Ansorge because, in the instant case, the claims specify that the inhibitors are

administered to an individual in need of the recited therapy." Applicant further argues that "arteriosclerosis is an inflammatory disease, but is not a dermatological disease, and is not caused by proliferation of fibroblasts." Applicant argues that "in connection with the cited reference of Ansorge et al, Applicants refer to U.S. counterpart, U.S. Patent No. 7,229,969, and points out Table 1 of the patent No. '969, which discloses diseases related to hyperproliferation of keratinocytes." Applicant argues that "the dermatological disease disclosed in the 7,229,969 patent are distinct from diseases caused by a hyperproliferation of fibroblasts, namely hypertrophic scars, keloids, sclerodermia, etc, which are caused by hyperproliferation and changed differentiation states of fibroblasts."

6. Applicant's arguments have been fully considered but have not been found persuasive. Ansorge reference teaches all of the active methods of the instant claims. Ansorge et al teach the combined used of DP IV inhibitor (Lys[Z(NO_2)]thiazolidide) and APN inhibitor (actinonin) for the treatment of atherosclerosis and dermatological diseases associated with hyperproliferation of keratinocytes. The reference teaches that the administration of the combination therapy inhibits DNA synthesis. Although Table 1 of Ansorge reference is not identical with the diseases treated by instant application, there is sufficient evidence that both keratinocyte and fibroblasts are involved in the diseases disclosed by Table 1 of Ansorge reference instant claims. In other words, there is sufficient evidence of similarity which is deemed to be present between the instantly claimed invention of claims 5, 13, 22 and 24 and the WO 02/053170 (or equivalence '969). For further support, see the references of record (Andriessen et al or

Machesney et al or Castagnoli et al). These references clearly discloses that keratinocyte and fibroblasts are involved in benign fibrotic and sclerotic diseases (post-infectious and post-traumatic, hypertrophic scars, keloids). Hypertrophic scars and keloids, for example, are diseases characterized by both proliferation of keratinocytes and fibroblasts, and as such, using the same compound (i.e., compounds claimed and disclosed in WO 02/053170 or '969, as Applicant pointed out), would inherently must treat benign fibrotic and sclerotic diseases, because it is the same population being treated (i.e., patients having disease pattern and/or condition associated with hypertrophic scars and keloids) in both situations.

Therefore, in the absence of evidence to the contrary or specific structural limitations, the prior art teachings clearly discloses the use of the claimed compounds to treat dermatological disease conditions of benign fibrotic and sclerotic diseases which include hypertrophic scars and keloids in a patient as well as to inhibit the activation of DNA synthesis of proliferation of human fibroblasts, and as such anticipates claims 5, 13, 22 and 24.

With respect to “wherein the therapy comprises an inhibition of activation, DNA synthesis and proliferation of human fibroblasts” according to MPEP 2111.04: "Claim scope is not limited by claim language that suggests or makes optional but does not require steps to be performed, or by claim language that does not limit a claim to a particular structure. However, examples of claim language, although not exhaustive, that may raise a question as to the limiting effect of the language in a claim are:

(A) “adapted to” or “adapted for” clauses;

(B) "wherein" clauses; and

(C) "whereby" clauses.

The determination of whether each of these clauses is a limitation in a claim depends on the specific facts of the case. In *Hoffer v. Microsoft Corp.*, 405 F.3d 1326, 1329, 74 USPQ2d 1481, 1483 (Fed. Cir. 2005), the court held that when a "whereby' clause states a condition that is material to patentability, it cannot be ignored in order to change the substance of the invention." Id. However, the court noted (quoting Minton v. Nat'l Ass'n of Securities Dealers, Inc., 336 F.3d 1373, 1381, 67 USPQ2d 1614, 1620 (Fed. Cir. 2003)) that a "whereby clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited." Id. <". In the instant case, it is not deemed that the "wherein" clause limits the claim to particular structural features.

New Objection

7. Claim 5 is objected to for the following minor informality: claim 5 contains the acronym "VCREST", and an acronym in the first instance of claims should be expanded upon/spelled out with the acronym indicated in parentheses, i.e., Calcinosis Raynaud's Syndrome Esophageal Dysmotility Sclerodactyly Telangiectasia (CREST). The abbreviations can be used thereafter.

8. Claim 5 is objected to for the following minor informality: There appears to be a mismatch in parenthesis. Claim 5 recites, "…and of rare localized fibroblast diseases (Dupuytren's disease…(Peyronie's disease, induratio penis plastica), comprising…" The

first parenthesis does not match with the second parenthesis, since the second parenthesis covers (Peyronie's disease, induratio penis plastica). This error should be corrected.

9. The abstract is objected to for the following minor informality:

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

In the instant case, the abstract recites, "The invention relates to a process for the inhibition…" at line 1 of the abstract. Further, at line 2, the abstract recites, "more specifically, the method is directed to..." Applicant should correct this informality. See MPEP 608.01(b). For example, the first line of the abstract should be corrected to "A process for the inhibition of the DNA synthesis…is provided."

New Rejection

35 U.S.C. 112, 2nd

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 5 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

12. Claims 5 recites parenthetical expressions (post-infectious and post-traumatic: hypertrophic scars, keloids, dermatofibromas, fibrolipomes, disseminated (myo)-fibromatoses), " “(fibrosarcomes, mixed tumors as atypical fibroxanthoma, malign fibrous histiocytoma, aggressive angiomyxoma, paraneoplasiae)”, “(circumscript sclerodermia, progressive-systemic sclerodermia, CREST syndrome),” “(white spot disease Lichen sclerosus et atrophicus),” "(eosinophilic/proliferative fascitis, pseudosclerodermiae generated by exogenous causes, such as, toxic oil syndrome, silicosis, porphyriae, eosinophilic myalgia syndrome, popular mucinosis (Lichen myxo-edematosus) or Borrelias-associated fibrosis states),” "(alopecia androgenetica),” “(Dupuytren’s disease, Ledderhose's disease, “knuckle pads”, penile induration (Peyronie’s disease, induratio penis plastica)" throughout the claim. The metes and bounds of Claim 5 is rendered vague and indefinite by the parenthetical recitation because it is unclear as to whether the limitation is part of the instantly claimed subject matter.

13. Claim 22 recites, "...α-amino phosphinic acid derivatives." It is unclear what compounds are encompassed within α-amino phosphinic acid derivatives. The dictionary defines “derivative" as “a chemical substance derived from another substance either directly or by modification or partial substitution” (see p. 3 from http://cancerweb.ncl.ac.uk/cgi-bin/omd?query=derivative). Since a derivative is a substance derived from another substance either directly or by modification or partial substitution, it is unclear what modifications or from which “another substance” are encompassed within alpha-amino phosphinic acid derivatives.

Conclusion

14. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JULIE HA whose telephone number is (571)272-5982. The examiner can normally be reached on Mon-Thurs, 5:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner’s supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Julie Ha/
Examiner, Art Unit 1654